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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/553,307

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John C. Gebler

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EXAMINER

XU, XIAOYUN

ART UNIT

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/553,307	<b>Applicant(s)</b> GEBLER ET AL.	
	<b>Examiner</b> ROBERT XU	<b>Art Unit</b> 1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 13 July 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) 4-13, 15-18, 48, 49, 52, 58-60, 66, 70-72, 84-87, 90, 91 and 93 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3, 23, 24, 37, 41, 44, 46, 50, 51, 56, 57, 65, 69, 73, 77, 79, 83 and 88 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 14 October 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>12/15/2005</u> . | 6) <input type="checkbox"/> Other: _____  |

Continuation of Disposition of Claims: Claims pending in the application are 1-13,15-18,23,24,37,41,44,46,48-52,56-60,65,66,69-73,77,79,83-88,90,91 and 93.

### **DETAILED ACTION**

1. Applicant's election without traverse of group I comprising claims 1-3, 23, 24, 37, 41, 44, 46, 48-51, 56, 57, 65, 69-73, 77, 79, and 83-88, and election with traverse of species in the reply filed on 07/13/2009 is acknowledged. The traversal is on the ground(s) that the various species are so linked as to form a single general concept. For example, with regard to claims 23 and 24, the aryl groups (claim 23) necessarily encompass heteroaryl groups (claim 24). This is not found persuasive because the claimed aryl groups have different chemical structures and properties than heteroaryl groups, they are patentably distinguishable and require different search. The requirement is still deemed proper and is therefore made FINAL.

The Examiner also realizes that Claims 48 and 49 were mistakenly grouped with wrong group (group I). Claims 48 and 49 depend on Claim 4. Claim 4 belongs to group II. Therefore, Claims 48 and 49 belong to group II and are withdrawn along with group II. Applicants are requested to indicate this change in the next response.

Thus, Claims 1-13, 15-18, 23, 24, 37, 41, 44, 46, 48-52, 56-60, 65, 66, 69-73, 77, 79, 83-88, 90, 91 and 93 are pending in the application, of which Claims 1-3, 23, 24, 37, 41, 44, 46, 50, 51, 56, 57, 65, 69, 73, 77, 79, 83 and 88 are considered on merits, Claims 4-13, 15-18, 48, 49, 52, 58-60, 66, 70-72, 84-87, 90, 91 and 93 are withdrawn from consideration as directed to non-elected invention.

### ***Claim Rejections - 35 USC § 102***

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-3, 23, 24, 37, 41, 44, 46, 51, 56, 57, 65, 69, 73, 77, 79, 83 and 88 are rejected under 35 U.S.C. 102(b) as being anticipated by Huang et al (Analytical Biochemistry, 1999, IDS) (Huang).

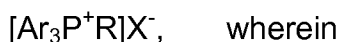
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In regard to Claim 1, Huang teaches a method of preparing a sample for mass spectrometry analysis. The method comprises:

- a) obtaining a sample comprising an analyte (peptide from tryptic digested protein), the analyte comprises an exposed group (NH<sub>2</sub>-terminus) (see page 307, right col. 2<sup>nd</sup> paragraph); and
- b) reacting the analyte (peptide) with a triarylphosphonium labeling reagent (Tris(trimethoxyphenyl)phosphonium (TMPP) reagents) having a reactive group (acetyl-O-succinimide (AcOSu)) capable of reacting with the exposed group (NH<sub>2</sub>-terminus) to form a triarylphosphonium-linked analyte (see page 307, right col. 3<sup>rd</sup> paragraph).

In regard to Claim 2, Huang teaches that the method comprising the further step of obtaining the triarylphosphonium labeling reagent having a reactive group (see page 307, left col. 3<sup>rd</sup> paragraph).

In regard to Claim 3, Huang teaches that the labeling reagent has a structure according to the formula



each Ar is an aryl group (methoxyphenyl) (see Scheme 1);

P is a phosphorous atom (see Scheme 1);

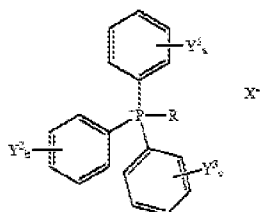
R is a reactive group comprising a functional group (AcOSu) that react with the exposed group (NH<sub>2</sub>-terminus) to form a covalent bond thereby forming triarylphosphonium-linked analytes (TMPP-Ac-peptide) (see Scheme 1); and

X<sup>-</sup> is a negatively-charged counter ion (Br<sup>-</sup>) (see Scheme 1).

In regard to Claim 23, Huang teaches that the Ar group is substituted aryl group (methoxyphenyl) (see Scheme 1).

In regard to Claim 37, Huang teaches that Ar<sub>3</sub>P group is substituted triphenylphosphophine (trimethoxyphenylphosphine) (see Scheme 1).

In regard to Claim 41, Huang teaches that the labeling reagent has a structure according to the formula



wherein

P is phosphorous atom (see scheme 1);

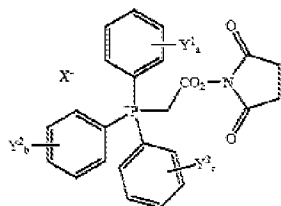
R is a reactive group (AcOSu) comprising a functional group that reacts with the exposed functional group (NH<sub>2</sub>-terminus) to form a covalent bond thereby forming triarylphosphonium-linked analytes (see scheme 1);

a, b, and c are 1 (see scheme 1);

Y<sup>1</sup>, Y<sup>2</sup>, and Y<sup>3</sup> are alkoxyl (see scheme 1);

X<sup>-</sup> is a negatively-charged counter ion (Br<sup>-</sup>) (see scheme 1).

In regard to Claim 44, Huang teaches that the labeling reagent has a structure according to the formula (TMPP-Ac-O-Su) (see Reagent 2 in scheme 1).



In regard to Claim 51, Huang teaches that the exposed group of the analyte (N-terminal group of peptide) is electrophilic and the reactive functional group (O-succinimide (OSu)) is nucleophilic (see scheme 1).

In regard to Claim 56, Huang teaches that X<sup>-</sup> is a halide (Br<sup>-</sup>) (see scheme 1).

In regard to Claim 65, Huang teaches that the labeling reagent has the following structure:



wherein

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each Ar is aryl group (methoxyphenyl) (see scheme 1);

P is a phosphorous atom (see scheme 1);

Z is a linking group (Ac) (see scheme 1); and

$\Psi$  is a reactive functional group (OSu) (see scheme 1).

In regard to Claim 73, Huang teaches that  $\Psi$  group is an isocynate (OSu) (see scheme 1).

In regard to Claim 77, Huang teaches that  $\Psi$  group is an aryl halide ( $\text{SC}_6\text{F}_5$ ) (see scheme 1).

In regard to Claim 79, Huang teaches that Z has 3 nonhydrogen atoms selected from group consisting of C, N, O and S, and the longest liner segment contains 2 nonhydrogen atoms (see scheme 1).

In regard to Claim 83, Huang teaches that the analyte is a peptide (see scheme 1, page 307).

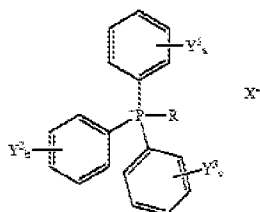
4. **Claims 1, 41, and 50** are rejected under 35 U.S.C. 102(b) as being anticipated by Leavens et al (Rapid Communications in Mass Spectrometry, 2002, IDS) (Leavens).

In regard to Claim 1, Leavens teaches a method of preparing a sample for mass spectrometry analysis. The method comprises:

a) obtaining a sample comprising an analyte (amines) (see table 1), the analyte comprises an exposed group (amine group) (see page 439, right col. 1<sup>st</sup> paragraph); and

b) reacting the analyte (peptide) with a triarylphosphonium labeling reagent (TMPP-reagents) having a reactive group (carboxylic group) capable of reacting with the exposed group (amine group) to form a triarylphosphonium-linked analyte (see Table 3, page 439, right col. 1<sup>st</sup> paragraph).

In regard to Claim 41, Leavens teaches that the labeling reagent has a structure according to the formula



wherein

P is phosphorous atom (see scheme 1);

R is a reactive group comprising a functional group (carboxylic group) that reacts with the exposed functional group (amine group) to form a covalent bond thereby forming triarylphosphonium-linked analytes (see Table 3);

a, b, and c are 3 (see scheme 1);

Y<sup>1</sup>, Y<sup>2</sup>, and Y<sup>3</sup> are alkoxy (see scheme 1);

X<sup>-</sup> is a negatively-charged counter ion (Br<sup>-</sup>) (see scheme 1).

In regard to Claim 50, Leavens teaches stable isotopically labeling of TMPP 'tag' with <sup>13</sup>C and <sup>2</sup>H for mass spectrometry analysis of target molecule (see abstract).

### ***Claim Rejections - 35 USC § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. **Claim 88** is rejected under 35 U.S.C. 103(a) as being unpatentable over Huang.



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In regard to Claim 88, Huang does not specifically teach that the sample is a biological tissue. It is well known that proteins can be obtained from biological tissue. At the time of the invention it would have been obvious to one of ordinary skill in the art to analyzing proteins obtained from a biological tissue.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT XU whose telephone number is (571)270-5560. The examiner can normally be reached on Mon-Thur 7:30am-5:00pm, Fri 7:30am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Vickie Kim can be reached on (571)272-0579. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

8/8/2009

/Yelena G. Gakh/  
Primary Examiner, Art Unit 1797

RX